REMARKS

Claims 1-8 and 10-15 were presented for examination, and were rejected. Claim 1 has been amended to incorporate the additional limitation from dependent claim 7. The amendment thus adds no new matter. Claim 7 was canceled in view of the amendment; claim 6 was also canceled. The amendment is believed to place the claims in condition for allowance, and it at least reduces the issues for and places the application in better form for appeal. Entry of the amendment and reconsideration are therefore respectfully requested.

Anticipation Rejections under 35 U.S.C. 102

Claims 1-3 and 6-15 were rejected as allegedly anticipated by Gao, et al. The applicant traverses that rejection as it could be applicable to the claims as now amended.

As a preliminary matter, the anticipation rejection was directed solely to claims 1-3 and 6-15: it was not applied to claims 4-5. Claims 4 and 5 were only rejected based on alleged obviousness (see below). Claim 7 was not subject to the obviousness rejection, so its added limitation, requiring the claimed assay control to be lyophilized, is not obvious in view of the cited references. The amendment of claim 1 now introduces a non-obvious limitation from claim 7 into claims 4-5, which depend from claim 1; and they were acknowledged not to be anticipated by the cited reference. Claims 4 and 5 contain limitations that were not anticipated, and the amendment adds an additional limitation that was not deemed obvious; these claims are therefore believed to be free from all of the cited references and in condition for immediate allowance.

This is how the anticipation rejection was explained by the Examiner:

> Gao et al. teach a parathyroid hormone (PTH) assay control. The assay comprises a whole PTH component having amino acid 1-84 of PTH, and a fragment having amino acid 7-84 of PTH which falls within the recited range, i.e. spanning position 2 through position 33 of PTH of its N-terminal, and C-terminal spanning from 35 through position of 84 of PTH, where Gao et al. teach storing the PTH in lyophilized form, e.g. protein matrix base (See page 606, right column, Materials and Methods-Chemicals and Reagents). The ratio of the whole PTH to the 7-84 fragment is within a range of about 1% to 99% (see Figure 2).

Claim 7 was separately rejected as allegedly anticipated by Gao et al. With respect to the added limitation of claim 7, the rejection says this:

> With regard to claims 6-8, Gao et al. teach using lyophilized form for storage of the PTH components to prolong storage life of the PTH peptides. Supra.

The Gao reference discloses an assay control, in the Materials and Methods section that the Examiner mentioned. The section about controls from Gao says this:

> Standards and controls for the whole PTH IRMA were prepared by adding synthetic PTH(1-84) to a normal human serum that did not show any detectable PTH level with the intact PTH assay. The concentrations of the standard set were 0, 10, 16, 46, 165, 700, and 2300 pg/ml. All standards and controls were aliquoted, lyophilized, and stored at 2-8°C.

Gao, pg. 606 (emphases added).

This passage discloses certain 'standards and controls', and it says that those "standards and controls were prepared by adding synthetic PTH(1-84) to a normal human serum that did not show any detectable PTH level with the intact PTH assay." As this expressly says, the 'standards and controls' of the reference have only PTH(1-84), they do not include any PTH fragments; indeed Gao says that the serum used for them did not contain any PTH according to the 'intact PTH assay'. Therefore, the standards and controls of Gao do not anticipate claim 1.

As described by the Examiner, "The assay comprises a whole PTH…." However, the Materials and Methods passage describing 'standards and controls' does not disclose an 'assay': the assays are discussed in other parts of the reference.

The assay to which the Examiner apparently refers is summarized in Figure 2, which was also mentioned by the Examiner. However, the Examiner appears to misunderstand what Figure 2 discloses: it does *not* disclose an assay where PTH(1-84) is combined with PTH(7-84).

The description of the assay in Figure 2 demonstrates that the assay described in the Figure does not include both PTH and a PTH fragment in a single assay. The graphs in Figure 2

plot radioactivity detected by two different assay methods against the concentration of the PTH material that is being measured. As the text associated with Figure 2 indicates, one of the two lines in each graph refers to PTH(1-84) concentration (the filled circles), and the other line refers to PTH(7-84) concentration (the open circles).

The two graphs in Figure 2 represents two different radioimmunoassay methods: the two different methods use two different antibodies that bind to different epitopes of PTH, so the two assays recognize different PTH species. Figure 2 is presented as evidence that the radioimmunoassay represented in the top graph (Nichols' "intact PTH" assay) is inferior to the one in the lower graph ("whole PTH IRMA") for purposes of measuring PTH(1-84) in samples that may also contain PTH(7-84) The graphs demonstrate that the "intact PTH" assay (top graph) cannot distinguish PTH(1-84) from PTH(7-84). The "whole PTH IRMA" assay (lower graph), though, detects PTH(1-84) selectively, and does not detect PTH(7-84) even when a large amount of PTH(7-84) (10,000 pg/ml) is present. Figure 2 thus demonstrates that the radioimmunoassay used for the lower graph detects PTH(1-84) and does not cross-react with PTH(7-84).

Looking at either of the two graphs in Figure 2, the filled circles represent PTH(1-84), and the open circles represent PTH(7-84). The graphs show radioactivity measurements made with a radioimmunoassay. Each point plotted on the graph represents the radioactivity detected in a single sample, and each plot represents a measurement of a sample containing a known concentration of either PTH(1-84) or PTH(7-84), *not both*. This would be clear to the person of ordinary skill from reading the description of the assay, and from the purpose of Figure 2, which is presented to prove the difference in "assay specificity" for the two assay methods. Figure 2 demonstrates that one assay can distinguish between PTH(1-84) and PTH(7-84), while the other one cannot. See Gao at page 608, the last paragraph in the left column and Figure 2 in the right column.

The *filled* circles in Figure 2 represent one series of assays, each reporting the radioactivity detected from a sample having a known concentration of PTH(1-84); and the *open* circles represent a separate series of assays, each reporting the radioactivity detected from a sample having a known concentration of PTH(7-84). Contrary to what the Examiner seems to indicate,

none of the data points on either graph in Figure 2 represents an assay where PTH(7-84) was mixed with PTH(1-84). That would be contrary to the purpose of the Figure, which is to show that one of the assay methods gives the same result for either PTH(1-84) or PTH(7-84), while the other one specifically detects PTH(1-84) without detecting PTH(7-84).

Claim 1 has been amended to include the limitations of claim 7, which requires the claimed product to be lyophilized, and it still requires both whole PTH and a PTH fragment to be present. None of the assays in Figure 2 represents a composition containing both PTH(1-84) and PTH(7-84). Therefore, Figure 2 does not disclose the combination of PTH peptides required by claim 1: it does not disclose any composition having whole PTH *and* a PTH fragment. Figure 2 also clearly does not disclose a *lyophilized* composition with these two materials plus a protein matrix base, since it discloses data from a liquid-phase assay. See, e.g., the assay method described on pg. 607. And the Materials and Methods section that the examiner pointed to does not disclose a composition containing whole PTH and a PTH fragment. It discloses how PTH(1-84) and PTH(7-84) and other materials were obtained or synthesized, but it does not disclose a product containing PTH(1-84) and PTH(7-84) together. And the only composition described in the Materials and Methods section of Gao that is lyophilized contains *only* PTH(1-84), it does not contain a PTH fragment. In view of the amendment, the claims are not anticipated by Gao.

The burden of establishing grounds for any rejection is on the Examiner. Here, no proper anticipation rejection has ever been established. The Examiner has not shown that the 'Materials and Methods' section of Gao discloses a composition containing both a PTH fragment and whole PTH as required by claim 1. In fact, it describes certain 'standards or controls', but it says they contain only PTH(1-84), without any PTH fragments present. Figure 2 discloses assays of samples with known concentrations of either PTH(1-84) or PTH(7-84), not both together, and it does not disclose any lyophilized product as required by the amended claim 1. Accordingly, this rejection must be withdrawn.

Obviousness Rejections under 35 U.S.C. 103

Claims 1-6 and 11-15 were rejected as allegedly obvious in view of certain cited references. However, claim 7 was not rejected for obviousness, and is thus understood to be allowable over all cited references in view of the remarks above. Incorporation of the limitation of claim 7 into claim 1 thus overcomes the obviousness rejection of all pending claims, so this rejection can be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 532212001900. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: April 13, 2007

Respectfully submitted,

By /Michael G. Smith/
Michael G. Smith
Registration No.: 44,422
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, California 92130-2040
(858) 720-5113